REMARKS

Status of the Claims

Claims 1-11, 15-19, and 24-26 are currently pending and under examination. Claims 12-14 and 20-23 have been canceled without prejudice or disclaimer of the subject matter claimed therein. New claims 24-26 have been added. New claims 24-26 are directed to the same invention as claims 1-11 and 15-19, and therefore, should be examined with these claims.

Amendments to the Claims

Claims 1, 8, 15, 17, and 18 have been amended.

Claims 1, 17, and 18 have been amended to recite that the pineal gland is accessed dorsal to the confluence of sinuses. Representative support can be found in the specification at page 5, paragraph [0021] and at pages 18-19, paragraph [0086].

Claim 8 has been amended to re-phrase the original claim. Representative support can be found in the specification at page 8, paragraph [0037].

Claim 15 has been amended to remove the phrase "and/or separated."

Claims 17 and 18 have been further amended to recite that the pineal is exposed by pressing downward on the dorsal cerebellum. Representative support can be found in the specification at page 5, paragraph [0021] and at pages 18-19, paragraph [0086].

New claim 24 provides the step that the pineal is exposed by pressing downward on the dorsal cerebellum. Representative support can be found in the specification at page 5, paragraph [0021] and at pages 18-19, paragraph [0086].

New claim 25 provides that the skull is opened dorsal to the confluence of sinuses. Representative support can be found in the specification at page 5, paragraph [0021] and at pages 18-19, paragraph [0086].

New claim 26 provides that the hook is used to lift nonpineal tissue located below the confluence of sinuses. Representative support can be found in the specification at page 18, paragraph [0086].

The amendments to the claims do not introduce prohibited new matter.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

The present invention provides a method for determining whether an agent modulates a preselected biological condition controlled by the circadian clock.

The Office Action rejected claims 1-11 on the basis that the specification does not define adequately what an "agent" is. Applicant respectfully submits that the specification adequately defines the term "agent." For example, at page 13, [0062], the specification defines the term "agent" to include "pharmacologically active agents, therapeutic agents, biological molecules, amino acids...neuropeptides...mammalian tachykinins...agonists, antagonists and derivatives of all of the above." Also, the specification states that the term "agent" can be used interchangeably with "chemical" and "metabolite" (specification at page 8, at paragraph [0036]). Moreover, the claims require that the agent modulates a preselected condition controlled by the circadian clock. Thus, the claimed method is not directed to identifying any agent, but an agent that modulate a preselected condition controlled by the circadian clock.

Further, it is respectfully pointed out that the claimed invention is drawn toward a method of identifying an agent that modulates a preselected condition. The present invention is not directed to a product or a composition. Accordingly, the specification adequately provides written description for the claimed invention. Therefore, it is respectfully requested that this rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 8 is rejected under 35 U.S.C. § 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter regarded as the invention.

Claim 8 has been amended. Claim 8, as amended, provides that the modulated preselected biological condition is the physiological state of a tissue.

The Office Action alleges that physiology is the study of the functioning of living organism and cannot be a condition. Claim 8, as amended, recites "physiological state of a tissue." The specification defines "biological condition" as referring to "the biological mode, situation, state, status or environment" and that a biological condition "may be the state of a

particular tissue" (page 8, [0037]). The physiological state of a tissue refers to the state of the tissue under normal physiological conditions. It is therefore respectfully submitted that claim 8, as amended, particularly points out the subject matter regarded as the claimed invention. Accordingly, it is respectfully requested that this rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-11 and 15-19 are rejected under 35 U.S.C. § 103(a) as obvious over Drijfhout *et al.* (J Pineal Res 20(1): 24-32, 1996), in view of Arendt (Reviews of Reprod 3: 13-22, 1998) and in further view of Sun *et al.* (PNAS 99(7): 4689-4691, 2002).

The present invention provides a method for determining whether an agent modulates a preselected biological condition controlled by the circadian clock. The present invention provides a method for accessing the pineal gland utilizing an access point dorsal to the confluence of sinuses and provides access by lifting the dural tissue below the confluence of sinuses and pressing down on the dorsal cerebellum to expose the pineal gland. The present invention provides a method wherein little to no damage of non-pineal tissue is sustained.

The Office Action alleges that these references render the claimed method obvious. Drijfhout *et al.* disclose a method of studying melatonin levels, wherein the pineal gland is accessed by threading a microdialysis tube transversely through each side of the temporal bone thereby piercing the non-pineal tissue enveloping the pineal gland. Drijfhout *et al.* do not disclose opening the skull at all. Drijfhout *et al.* disclose an entirely different method of accessing the pineal, a method whereby tissue surrounding the pineal is inevitably injured as the mircodialysis tube and the threading wire must inherently pierce it in threading the tube through the brain. Furthermore, the present invention provides a method capable of constant recovery and monitoring in long term studies, which is required for "circadian clock" studies. (*See e.g.* specification at [0009} on pages 2-3, and claim 19). Drijfhout *et al.* disclose a method wherein the animals are sacrificed the day after surgery, a method unsuitable for constant recovery and monitoring over long periods of time. (*See* Drijfhout *et al.* at page 25, right column, under heading "Surgery" and at page 26, right column, first full paragraph).

Arendt discloses a review of melatonin's role in circadian rhythm. Arendt does not

disclose any surgical methods, but instead provides a review of using locomotor activity as a marker for measuring melatonin's effects. Sun *et al.* disclose a surgical method wherein the pia mater is actually removed, a step that is irrevocably harmful to the non-pineal tissue (*see* Sun *et al.* at page 4686, right column under "Surgery"). In contrast, the present invention does not require removing the non-pineal tissue.

Moreover, claims 1, 17, and 18, as amended, as well as claims 2-11, 19, and 24-26 which depend directly or indirectly thereon, provide a method of inserting a monitoring device into or near the pineal gland, wherein the pineal gland is accessed by opening the subject's skull at a point dorsal to the confluence of sinuses. The cited references do not disclose opening the skull at this point. Furthermore, the cited references do not teach lifting the nonpineal tissue with a hook or exposing the pineal gland by pressing down on the dorsal cerebellum.

Claim 15, as well as claim 16 which depends from claim 15, provides an improved surgical method, the improvement comprising a circular dental disk drill to open the skull, and a hook to lift nonpineal tissues away from the pineal. Drijfhout *et al.* teach drilling two temporal holes and threading microdialysis tubing through with the use of wire. Sun *et al.* teach drilling a single hole and removing the pia mater. Arendt is silent with regard to surgical methods. The cited references neither disclose using a hook to lift the nonpineal tissue nor teach lifting the dura tissue below the confluence of sinuses.

Accordingly, there is no motivation to combine the cited references and to modify the teachings of the cited references to arrive at the claimed invention with a reasonable expectation of success. It is therefore respectfully requested that the rejection of claim 1-11 and 15-19 under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicant respectfully requests entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please

charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

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Respectfully submitted,
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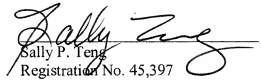

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